Reward System in children and adolescents with ADHD and Anxiety disorders

Luigi Mazzone

New York, Italian Academy for Advanced Studies in America
November 1, 2006

Anxiety disorders and Attention Deficit Hyperactivity Disorder (ADHD) are highly prevalent childhood disorders and their symptoms can negatively interfere with general well-being, social life, academic performance, and development of social skills (Pine et al. 1998, Kendall et al. 2001, 2004). In the U.S, the prevalence of anxiety disorders has been estimated to be 5.7% in a cohort aged 9-13 yrs (Costello et al. 1996, 2003) and 13.0% in a cohort aged 9-17 yrs (Shaffer et al. 1996).

The neurobiology underlying the two disorders is only partially understood. An alteration of the reward system is supposed to be critical in ADHD leading to a bias toward approach behaviour, whereas perturbation in this system could contribute to the avoidance behaviour characteristic of anxious individuals

Children with ADHD require stronger and more salient reinforcers to regulate their behavior than do healthy children, yet they respond excessively to novel stimuli as rewarding stimuli, i.e., generating approach behavior, often indiscriminately. They show less sensitivity to changes in reinforcement contingencies, and respond more strongly to negative than positive reinforcers (Ernst 2003). Neural correlates of behavioural control has been placed on neural circuits involving dorsolateral prefrontontal (DLPFC) and anterior cingulated cortex (ACC). The ACC, especially the dorsal ACC, has strong connections to the DLPFC and is considered to play a critical role in complex cognitive processing (Bush et al 2000), particularly target detection, response selection, error detection, and reward-based decision-making (Bush et al 2002), functions that are thought to be impaired in ADHD.

In contrast, anxiety disorders are characterized by a bias towards harm-avoidant behaviors. An obvious difficulty in the study of anxiety is the heterogeneity of disorders placed under the umbrella of anxiety disorders. Nonetheless, several theoretical models of generic anxiety have been proposed that focus on the interaction between cognition, affect, physiology, and behavior (for review, Wilken et al 2000). The association of stimuli with adverse affective experiences is a critical determinant of hyperarousal (Dowden and Allen 1997) and anxious apprehension, which occur across anxiety disorders. Accordingly, the neural substrates engaged in the processing of aversive stimuli have been implicated in the pathophysiology of anxiety. These include limbic (amygdala, ventral striatum) and paralimbic structures (orbitofrontal cortex, insula, ACC) (Ernst et al., 2003). Although a voluminous literature attributes a specialized role for harm avoidance to the amygdala (LeDoux, 2000) and for reward processing to the nucleus accumbens (Wise et al. 1992; Di Chiara, 2002), these structures support a number of additional functions, such as associative learning (Cardinal et al. 2002b; Salamone & Correa, 2002; Gabriel et al. 2003) and attention filtering (Pessoa & Ungerleider, 2004), which are perturbed in both ADHD and anxiety disorders.

Although anxiety appears to be biased toward avoidance and ADHD towards approach behaviour, these two disorders often coexist within individuals. Approximately 25% of children with ADHD have an anxiety disorder (Pliszka et al, 1999; Levy et al. 2004).

The aim of the present project is to explore alteration in the reward system in patients with ADHD and Anxiety disorder compared to healthy controls. Unique patterns of activity in the reward system could be helpful in understanding how this system contributes to motivated behaviour. In addition, a better understanding of the underlying neurobiological substrates of anxiety and ADHD should provide a priori hypotheses for future focused studies.

References

Pine DS, Cohen P, Gurley D, Brook J, Ma Y (1998), The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. Arch Gen Psychiatry 55:56–64

Kendall PC, Brady EU, Verduin TL (2001), Comorbidity in childhood anx-iety disorders and treatment outcome. J Am Acad Child Adolesc Psychiatry 40:787–794

Kendall PC, Safford S, Flannery-Schroeder E, Webb A (2004), Child anxiety treatment: outcomes in adolescence and impact on substance use and depression at 7.4-year follow-up. J Consult Clin Psychol 72:276–287

Costello EJ, Mistillo S, Erkanli A, Keeler G, Angold A (2003), Prevalence and development of psychiatric disorder in childhood and adolescence. Arch Gen Psychiatry 60:837-844.

Costello EJ, Angold A, Burns BJ, et al. (1996), The Great Smoky Mountains Study of Youth. Goals, design, methods, and the prevalence of DSM-III-R disorders. Arch Gen Psychiatry. 1996 Dec;53(12):1129-36.

Shaffer D, Fisher P, Dulcan MK, Davies M, Piacentini J, Schwab-Stone ME, lahey BB, Bourdon K, Jensen JS, Bird HR, Canino G, Regier DA (1996), The NIMH Diagnostic Interview Schedule for Children Version 2.3 (DISC-2.3): description, acceptability, prevalence rates, and performance in the MECA Study. Methods for the Epidemiology of Child and Adolescent Mental Disorders Study. J Am Acad Child Adolesc Psychiatry. 35:865-877.

Ernst M, Grant SJ, London ED, Contoreggi CS, Kimes AS, Spurgeon L. Decision making in adolescents with behavior disorders and adults with substance abuse. Am J Psychiatry. 2003 Jan;160(1):33-40.

G. Bush, P. Luu and M.I. Posner, Cognitive and emotional influences in anterior cingulate cortex, *Trends Cogn Sci* **4** (2000), pp. 215–222

G. Bush, B.A. Vogt, J. Holmes, A.M. Dale, D. Greve, M.A. Jenike and B.R. Rosen, Dorsal anterior cingulate cortex: a role in reward-based decision making, *Proc Natl Acad Sci U S A* 99 (2002), pp. 523–528

Wilken JA, Smith BD, Tola K, MannM(2000): Trait anxiety and prior exposure to non-stressful stimuli: Effects on psychophysiological arousal and anxiety. *Int J Psychophysiol* 37:233–242.

Dowden SL, Allen GJ (1997): Relationships between anxiety sensitivity, hyperventilation,and emotional reactivity to displays of facial emotions. *J Anxiety Disord* 11:63–75.

Ernst M, Kimes AS, London ED, Matochik JA, Eldreth D, Tata S, Contoreggi C,
Leff M, Bolla K. Neural substrates of decision making in adults with attention deficit hyperactivity disorder. Am J Psychiatry. 2003 Jun;160(6):1061-70.

LeDoux, J. E. (2000). Emotion circuits in the brain. Annual Review of Neuroscience 23, 155–184

Wise, R. A., Bauco, P., Carlezon Jr., W. A. & Trojniar, W. (1992). Self-stimulation and drug reward mechanisms. Annals of the New ork Academy of Sciences 654, 192–198.

Di Chiara, G. (2002). Nucleus accumbens shell and core dopamine: differential role in behavior and addiction. Behavioural Brain Research 137, 75–114.

Cardinal RN, Winstanley CA, Robbins TW, Everitt BJ.
Limbic corticostriatal systems and delayed reinforcement.
Ann N Y Acad Sci. 2004 Jun;1021:33-50. Review.

Salamone, J. D. & Correa, M. (2002). Motivational views of reinforcement: implications for understanding the behavioral functions of nucleus accumbens dopamine. Behavioural Brain Research 137, 3–25.

Gabriel, M., Burhans, L. & Kashef, A. (2003). Consideration of a unified model of amygdalar associative functions. Annals of the New York Academy of Sciences 985, 206–217.

Pessoa, L. & Ungerleider, L. G. (2004). Neuroimaging studies of attention and the processing of emotion-laden stimuli. Progress in rain Research 144, 171–182.

Pliszka SR, Carlson CL, Swanson JM (1999). ADHD with Comorbid Disorders: Clinical Assessment and Management. Guilford Press: New York.

Levy F. Synaptic gating and ADHD: a biological theory of comorbidity of ADHD and anxiety. Neuropsychopharmacology. 2004 Sep;29(9):1589-96. Review.